COMPARABILITY ASSESSMENT OF AN ANTIBODY-DRUG CONJUGATE (ADC)

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In order to manufacture material for late-stage clinical trials and in preparation for the development of commercial manufacturing, several changes were implemented for the manufacture of the antibody intermediate (Ab), the ADC drug substance (DS) and drug product (DP). A risk assessment was performed before the implementation of the changes and the study indicated that the changes were of low to medium risk.

The antibody intermediate manufacturing process was optimized to increase robustness and yield. The storage concentration of the Ab was increased six fold and a suitable formulation for the increased concentration was also implemented. The comparability of the two post-change Ab lots was assessed by using release and characterization tests. For the release tests, pre-defined comparability target ranges were established based on the results obtained with the pre-change GMP batches and based on our understanding of the impacts of the quality attributes on safety and efficacy of the drug product. Besides the two post-change Ab lots, characterization testing was also performed, side-by-side, on three pre-change GMP Ab lots and the all the results were required to pass the pre-defined comparability target ranges. The study indicated that the post-change antibody intermediate was comparable to the pre-change Ab.

The ADC drug substance manufacturing process was scaled up. The comparability of the ADC DS was based on the assessments of a) the release results, b) side-by-side characterization testing, and c) side-by-side forced degradation testing of the post-change and pre-change lots. The review of the acquired data indicated that the post-change ADC DS was comparable to the pre-change material.

The ADC DP is stored in type I glass vials. The fill/finish process was also scaled up. The ADC DP has the same composition as the ADC DS. Since comprehensive comparability was performed for the ADC DS, the assessment of comparability of the ADC DP was performed by comparing only the release results to pre-defined comparability target ranges derived from the testing results of representative pre-change GMP lots.

Additionally, the antibody intermediate, the ADC DS and the ADC DP lots were placed on long term stability and their stability trends will be closely monitored.

The presentation will summarize our strategy and results of this ongoing comparability exercise.